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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/084,638
Filing Date: February 27, 2002
Appellant(s): BABICH, MICHAEL

Alice O. Martin
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/11/2007 appealing from the Office action mailed 01/11/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,583, 046	Valenta et al.	12-1996

Vrtala, S. et al. 'Induction of IgE Antibodies in Mice and Rhesus Monkeys with Recombinant Birch Pollen Allergens: Different Allergenicity of Bet v 1 and Bet v 2. J. Allergy. Clin. Immunol. 98(5):913-921, 1996.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 17 and 22-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,583,046 (Reference A1 on the IDS filed on 12/09/2002) as evidenced by Vrtala et al. (Reference AR on the IDS filed on 08/06/2002).

U.S. Patent 5,583,046 teaches obtaining and administering the recombinant or synthetic P14 allergen (which is the same applicants recited sequences for Bet v2, a profilin) in pharmaceutically acceptable carriers, into patients to diagnostically determine allergenicity to said protein (In particular, column 2, line 63 to column 4, line 36). The reference is silent as to whether the Bet v2 is multimeric.

Vrtala et al. teaches that Bet v2 naturally polymerizes in solution to form stable polymers. (In particular, results section of abstract). On page 914, the reference teaches "it could be shown that rBet v2 formed polymers through disulfide bonds" and that "the tendency of recombinant Bet v2 to form polymers through disulfide bonds under non-reducing conditions was demonstrated by SDS-PAGE, immunoblotting and blot overlays" (In particular, last paragraph of left column and second paragraph of right column) Vrtala et al. is only being used as an

evidentiary reference to illustrate an already described process showing inherent properties of the molecule.

It is noted that claim 25 is included in the rejection since any fragment of Bet v2 would inherently have novel sequences that arise from polymerization because the starting material for polymerization is identical. Since the fragments of claim 25 are recited with "comprising" language the claim reads upon the full length Bet v2 prior art protein of U.S. Patent 5,583,046

The prior art teachings anticipate the claimed invention.

(10) Response to Argument

On pages 3-4 of the Appeal Brief, Appellant argues the following:

> "35 U.S.C. §102 rejection is not supported because all of the steps recited in claim 17 are not taught by the '046 patent and using the Vrtala reference is improper to cure the deficiencies.
>
> On page 2 of the Action, the examiner rejected claims 17 and 22-28 under 35 U.S.C. §102 (b) as being anticipated by U.S. Pat. No. 5,583,046 (Valenta et al), "as evidenced by Vrtala *et al.*" The examiner has not established a legally sufficient basis for a 102 (b) rejection because neither Valenta et al. nor Vrtala et al. either singly or in combination teach all the claimed elements as required to anticipate. In addition, there is no justification for adding Vrtala to what should be a rejection based on a single case. Such a combination is an improper and an incorrect basis for an anticipation rejection. To stretch beyond one reference, the omitted element must be recognized in the art. The examiner has not demonstrated recognition of multimeric profilin as a hyposensitizing agent. Even if combined, the combination still does not teach all the elements of the pending claims. The examiner's sole reasoning in support of using Vrtala to fill in the admitted deficiencies in Valenta, is as follows:
>
> Vrtala recognized that when Bet v2 is placed in solution it naturally polymerizes. The Vrtala et al., reference is only relied upon to characterize an already described process.
>
> Office Action, page 2.

The examiner does not identify what "solution" in Valenta or in the pending application are being compared. There is no proof of an "already described process" that is the same as the claimed process.

A. Valenta does not teach the claimed elements

To anticipate, a **single reference must teach all the elements** of the claims. RCA *Corp v. Applied Digital Data Sys., Inc., 221* USPQ 385,388 (Fed. Cir. 1984). An anticipating prior art reference should disclose **each and every limitation** of the claim expressly or inherently. *Akamai Techs. v. Cable & Wireless Internet Servs.,* 344 F.3d 1186, 1192 (Fed. Cir. 2003). To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. PPG Industries, Inc. v. Guardian Industries Corp., 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996). (emphases added).

By the examiner's own admission, the '046 (Valenta) patent does not anticipate. The examiner admits that "Claim 17 requires .... administering a multimeric profilin" and also admits "The "046 patent .... is silent as to whether Bet v2 is multimeric."
As the examiner admits, the "046 patent does not disclose all the claim elements. For example, "046 does not disclose or even suggest the use of a multimeric profilin to hyposensitize a mammal. The "046 patent merely discloses a synthetic version of a 14 kDa birch pollen antigen P 14:

> The present invention provides recombinant DNA molecules which contain a nucleotide sequence that codes for a polypeptide which exhibits the same or similar antigenic properties as a natural allergen, P 14,... (Col. 2, lns. 14-17)

> The present invention covers the use of P14 synthetic polypeptide allergens to hyposensitize or desensitize a mammal. Such polypeptides can be administered to a human subject either alone or in combination with pharmaceutically acceptable carriers or diluents, in accordance with standard pharmaceutical practice. (Col. 11, Ins. 34-40)

In contrast, the claims of the present application are based, in part, on the increased IgE recognition of profilin multimers, singular fragments based on the sequence that uniquely may arise, or be exposed, upon profilin polymerization that are not available in the monomeric parent molecules. This may reflect one or more novel amino acid sequences that are comprised of part of each of at least two monomers complexed together to form the polymer, or a sequence that is buried within the tertiary monomeric structure that becomes exposed upon multimerization with one or more

additional profilins. Such fragments are not dependent upon whether a portion of IgE epitope(s) is present or not. The novel polymers of the present invention takes advantage of native configurations/structural phenomenon that lead to the pan-allergenic potential (not taught in the "046 patent) that, in turn, may be used for diagnostic and therapeutic use to induce a hypoallergenic response. "

Appellant's arguments have been fully considered, but are not found persuasive.

It is the Examiner's position that U.S. Patent 5,583,046 teaches obtaining and administering the recombinant or synthetic P14 allergen (which is the same applicants recited sequences for Bet v2, a profilin) in pharmaceutically acceptable carriers, into patients to diagnostically determine allergenicity to said protein (In particular, column 2, line 63 to column 4, line 36, column 11, lines 34-49). The reference is silent as to whether the Bet v2 is multimeric.

Vrtala et al. teaches that Bet v2 naturally polymerizes in solution (pharmaceutically acceptable solution injected into animals) to form stable polymers. (In particular, results section of abstract). On page 914, the reference teaches "it could be shown that rBet v2 formed polymers through disulfide bonds" and that "the tendency of recombinant Bet v2 to form polymers through disulfide bonds under non-reducing conditions was demonstrated by SDS-PAGE, immunoblotting and blot overlays" (In particular, last paragraph of left column and second paragraph of right column) Vrtala et al. is only being used as an evidentiary reference to illustrate an already described process showing inherent properties of the molecule.

Applicant argues that the reference is silent about the claimed multimeric profilin. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is

evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. The Examiner properly shifted the burden to applicant to establish, through objective evidence, that Bet v2 profilin of invention differs in unobvious manner from that of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993). Here, applicant has not provided any objective evidence to support a difference between the prior art P14 allergen and the instant multimeric Bet v2. The record does not contain sufficient objective evidence that the referenced P14 allergen differs in any significant manner from that claimed multimeric Bet v2.

The Examiner relied on Vrtala et al. as an evidentiary reference to show that Bet v2 naturally polymerizes in solution to form multimeric profilin in the instant rejection. However, the rejection could just as easily have been made by relying on the specification as evidence that that Bet v2 polymerizes to form multimeric profilin in solution because on page 10, lines 12-21 the specification discloses that biochemical data and computer-based modeling show that profilin can form multimers and that the multimers remain strongly attached due to strong chemical bonds and that "the chemical free energy (favorable state) for two profiling molecules is to self associate." The chemical free energy state is an inherent property of the molecule. When Bet v2 is placed in solution, as required to administer to a subject in non-lyophilized form, it polymerizes due to the physical properties of the molecule.

Further, the specification discloses on page 10, lines 12-13 that "the ability of plant profilin to form clinically relevant multimers from human and a variety of plant species is a novel aspect of the present invention." However, on page 11, lines 7-9, the specification discloses that "established methods of profilin isolation have often yielded extraneous and

unidentified proteins ...that are ≥2 times the recognized size of the 12-15 kDa cytoskeletal molecule." The court in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) held that "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." The prior art shows inherent characteristics of profilin that may have been unappreciated, but are nonetheless inherent properties of the molecule and are not patentably distinct.

On pages 5-7 of the Appeal Brief, Appellant argues the following:

B. The examiner has not countered applicant's assertion that Vrtala teaches away from the claimed invention

According to the examiner, Claim 17 requires an in vivo diagnostic test comprising administering a multimeric profilin molecule. "The '046 patent teaches administering Bet v2, a profilin. The reference is silent as to whether Bet v2 is multimeric." The examiner added Vrtala because of the statement that when rBet v2 is placed in solution, it naturally polymerizes.

There is no teaching in the '046 patent that when Bet v2 is placed in solution, as required to administer to a subject in non-lyophilized form, it polymerizes due to the physical properties of the molecule. The Vrtala reference teaches on page 914 "it could be shown that rBet v2 formed polymers through disulfide bonds" and that "The tendency of recombinant Bet v2 to form polymers through disulfide bonds under non-reducing conditions was demonstrated by SDS-PAGE, immunoblotting and blot overlays. The examiner's position is that "this reference has been used simply to illustrate an already described process showing inherent properties of the molecule."

Vrtala teaches against the present invention. For example, on page 914, left column, Vrtala states the following:

It could be shown that rBet v2 formed polymers through disulfide bonds, and it is hence suggested that the decreased allergenicity of rBet v2 might be related to its

tendency to polymerize. (emphasis added)

On page 920, left column, Vrtala further states the following:

[a]nd it is hence possible that the weaker capacity of rBet v2 to induce IgE antibodies might be linked to the ability to form natural polymers through disulfide bonds. Although it must be stressed that there is currently no feasible experimental data suggesting that polymerization of antigens might be a mechanism with which to reduce the allergenicity of protein antigens in favor of a TH 1 response. (emphasis added)

Therefore, Vrtala teaches away from the present invention which claims profilin multimers result in increased allergenicity. The utility of profilin multimers was not recognized in the references cited by the examiner nor are there arguments presented to pinpoint where in solutions of the publication multimeric profilin is formed, and to equate such multimers to those in the present claims.

Vrtala et al. did not find utility for profilin multimers in allergy diagnostics nor therapeutics; they state the opposite.

Their experimental approach does not indicate that profilin multimers would be more allergenic/antigenic and yield possible unique epitopes (upon multimerizing) that could be used as a basis to develop profilin multimer-based diagnostics and immunotherapeutics:

1) The form Vrtala injected into the animal models is not clear, but likely is a monomeric form. Conditions to make a soluble form were followed that would produce mostly monomeric profilin (in Methods: "The recombinant protein produced a single peak in the chromatogram obtained by high-pressure liquid chromatography and was completely soluble").

2) Production of a monomeric form (displayed in Figures 1 and 2) for injection is consistent with the production in animal models of monomeric-recognizing IgG and IgE (lesser degree) shown in Figure 3. Indeed, there were no noted antibodies that recognized the larger profilin forms.

3)20x of the profilin (Bet v2) was required vs. Bet v1: Vrtala's assumption is because it's due to "some intrinsic property", but "there is currently no feasible experimental model to definitively prove this hypothesis" (page 920, last paragraph).

Considering information in the present application, the reason 20x more of Bet v2 profilin vs. Bet v1 was needed by Vrtala to elicit a response was because the injected solution contained monomers (i.e., weaker allergen/antigen) or undetectably small

amounts of multimers such that a high concentration was needed to achieve an immune response.

Vrtala teaches away from the claimed invention. The form of rBet v2 injected into the animal models was likely monomeric. On page 914 in the Vrtala Methods section relied upon by applicant for this assertion, "the recombinant protein produced a single peak in the chromatogram"refers to the rBet v1 protein. There is not contrary data for rBet v2.

Therefore, Vrtala further illustrates contrasting conclusions to the present invention about the use of profilin multimers in diagnostics and therapeutics. The utility of profilin polymers was not recognized nor was it obvious that the profilin polymers would be a key allergen. "

Appellant's arguments have been fully considered, but they are not found persuasive. The Examiner has used Vrtala et al as an evidentiary reference only to show that Bet v2 inherently polymerizes in solution. *See MPEP 2131.01(c)* Vrtala et al. is only an evidentiary reference and is not part of the rejection. Therefore, whether the teachings of Vrtala et al. "teach away" from the instant claims is not relevant to the instant rejection. Appellants have acknowledged on pages 5-7 of the Appeal Brief that Bet v2 polymerizes when placed in solution. That fact alone is sufficient to show that the teachings of U.S. Patent 5,583,046 anticipate the claimed invention. Whether the authors of Vrtala et al. found that the polymerization decreased allergenicity or that the polymerized Bet v2 could be used for the purposes of the instant claims is not pertinent this rejection. Vrtala is being relied on to show inherent properties of the profilin Bet v2 molecule, not observations of the level of allergenicity of the profilin or any other teaching.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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December 18, 2007

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